PRIMARY EFFUSION LYMPHOMA OF PLASMABLASTIC TYPE: A RARE PRESENTATION IN AN IMMUNOCOMPETENT MALE ADULT

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ABSTRACT

A primary effusion lymphoma is a rare type of Non-Hodgkin's lymphoma where serous cavities are involved that cause peritoneal, pleural & pericardial effusions without any lymphadenopathy. They affect immunosuppressive patients with human Herpes virus 8 being the suspected aetiological agent. The prognosis is usually poor despite treatment. Here is a case of an immunocompetent patient with left-sided pleural effusion diagnosed as primary effusion lymphoma who presented with dry cough and breathlessness.

KEYWORDS
Primary Effusion Lymphoma, Human Herpes Virus-8.

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INTRODUCTION: CASE REPORT: A 66-year-old man with complaints of progressive breathlessness. Patient was a known hypertensive since 2002. The general condition of the patient was normal, vital signs were as follows: temperature 36.8^{0}C, heart rate-90/min., BP was 120/80 mmHg, RR-16/min. Physical examination revealed decreased breath sounds on the left side on auscultation of the chest. 2D Echo was suggestive of 70% ejective fraction and no regional wall motion/valvular abnormality. Chest X-ray revealed left-sided massive pleural effusion. Therapeutic pleurocentesis was done & fluid sent for investigations. The fluid reports showed ADA of 108 u/L which was lymphocytic predominant and exudative in nature. GeneXpert did not detect MTB and Serum ACE levels were 39.12. Cytological examination of pleural fluid showed atypical cells of haematolymphoid origin. No peripheral lymphadenopathy was detected.

Investigations:

Haemoglobin	11.7
Total WBC count	9600
Platelet count	610,000
Peripheral Smear-Neutrophils Lymphocytes Eosinophils	71% 21% 3%
Blood Glucose	120 mg/dL
Total Proteins	7.1
Serum albumin	3.2
Alkaline phosphatise	105
Pleural fluid-Cell counts Nature of fluid Proteins Lymphocyte Mesothelial cells	655 Haemorrhagic fluid 5.3 g/dL 90 3

Liver & renal function tests were normal.
Hepatic markers & HIV were negative.
Epstein Barr Virus immunoglobulin IgG-Positive.

Serum protein electrophoresis:

Total protein	7.4
Albumin	3.3
Alpha 1	0.27
Alpha 2	1.19 High
Beta	0.73 Low
Gamma	1.91 High
Myeloma band	Not detected

Serum Immunofixation:

IgG Band	Positive
IgM Band	Not detected
IgG Band	Not detected
Kappa band	Positive
Total IgA Total IgG Total IgM	1.81 20.20 High 0.43

CT Thorax showed left-sided moderate pleural effusion with minimal pericardial effusion (5 mm) in thickness. No hepatosplenomegaly. PET Scan showed left-sided pleural effusion with contralateral mediastinal shift. No focus of hypermetabolism in lung parenchyma or elsewhere in the body. Fig. 1 & 2.

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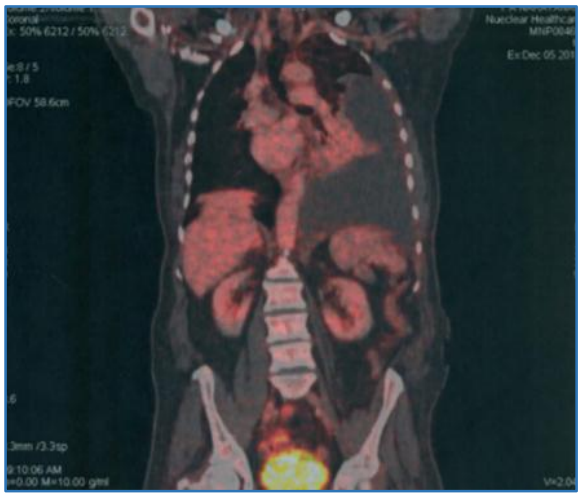

Fig 1

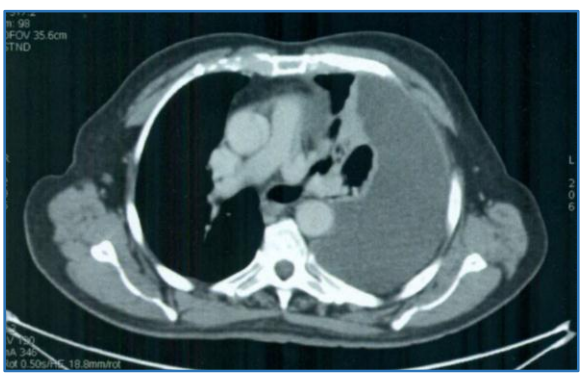

Fig 2

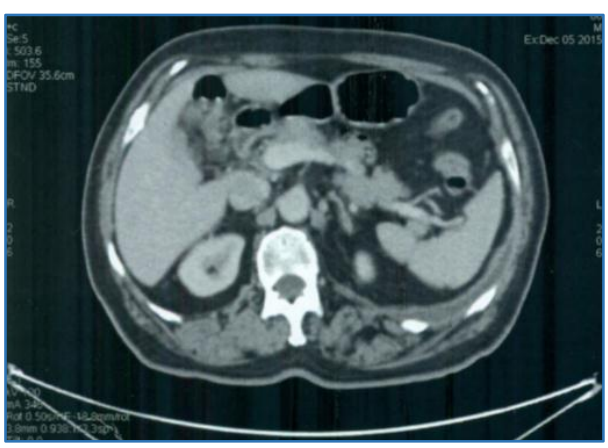

Fig 3

Bone marrow biopsy was done. Biopsy showed uninvolved marrow. Repeat pleurocentesis was done, the fluid of which showed cells of Non-Hodgkin's lymphoma, plasmablastic type. The tumour cells express CD -138, MUM 1, CD43 & CD30. They were immunonegative for CD20, CD-3, CD-79a, ALK-1, PAX-5 and HHV-8 LANA. EBV-RNAs by ISH were also expressed in the tumour cells. Thoracoscopic pleural biopsy was planned initially. However, could not be accomplished due to worsening general condition of patient. A COP-EPOCH chemotherapy protocol was administered. The patient was discharged with an appointment for the 2nd cycle of chemotherapy. However, patient failed to follow up for second cycle.

DISCUSSION: Due to its distinct biological and clinicopathological features, PEL has been recognised as an independent lymphoproliferative malignancy-with a large cell morphology, B-cell genotype and tendency to infiltrate serous mucosa causing effusions without any tumoural mass or LAP.[1-8] More specifically, it is defined as a lymphoma of the post-germinal centre, pre-terminally differentiated B-cells.[2] PEL became salient around 1995, after which there has been much effort to clarify its, yet uncertain, obscure pathogenesis. By and large, HHV-8 and EBV are the leading suspective aetiological factors.[1-5] HHV-8, also termed as Kaposi's sarcoma (KS)-associated herpes virus.[4,9] is a gamma herpes virus which encodes genes highly homologous to cytokine genes and genes closely related to cell cycle control.[4,9,10]

According to experimental studies, HHV-8 is also found to induce acceleration of the cell cycle and cell transformation or promote the proliferation of infected cells.[11,12] HHV-8 DNA is rarely found in various tumour and non-tumour tissues from patient groups not at risk of KS whereas it has been shown to be in exclusive association with KS, multicentric Castleman's disease and PEL but less so with multiple myeloma and sarcoidosis.[3,5,13,14] Despite the scepticism of its role in the pathogenesis of PEL, a concurrent EBV infection takes place in approximately 70% of patients.[4] It is also speculated that a pathological synergy exists between EBV and HHV-8 in the pathogenesis of PEL. In contrast to HIV-positive patients who are usually also EBV-positive, almost all HIV negative cases with PEL are EBV-negative.[5] Interestingly, EBV-RNA by immunohistochemistry was expressed in tumour cells in our patient.

In cases of PEL, immunophenotyping of the pleural fluid is characterised by the absence of cellular markers for the B and T cell lineages. The cells may be positive or negative for CD45 (a common pan-leukocyte antigen) and usually present cellular activation antigens, such as CD30, CD38, CD71 or HLA-DR. Antigens associated with T cells (such as CD2, CD3 and CD5) and antigens associated with B cells (such as CD19, CD20 and CD22) are invariably negative, as are the antigens HMB-45 and S-100.[15,16-17] The tumour cells express CD 138, MUM-1, CD 43 & CD 30. They were immunonegative for CD 20, CD 3 & CD 799, ALK-1, PAX-5 & HHV 8-LANA. When immunophenotyping is insufficient to determine the lineage of the tumour cells, gene rearrangement through molecular techniques is generally used to confirm the presence of clonality.[18]

Classified as a Non-Hodgkin's lymphoma, PEL affects the serous cavities. Since it is a rare pathology, there have been very few studies of its incidence. However, according to European data, PEL accounts for 3% of all Non-Hodgkin's lymphomas affecting patients with acquired immunodeficiency syndrome and for 0.4% of those affecting the seronegative population in general.[4,8] It is believed that the pathogenesis of PEL is multifactorial, and that the factors involved include breakdowns in the immune surveillance of

immunocompromised patients, as well as qualitative alterations in immunoregulation due to immunosenescence.[3]

Concomitance of chronic diseases is another potential risk factor. A diagnosis of pleural PEL is initially based on excluding the possibility of other lymphoproliferative diseases that affect the pleural cavity and result in pleural effusion. In order to eliminate the possibility of secondary involvement of the pleural cavity caused by lymphoma, it is recommended that computed tomography scans of the neck, chest and abdomen be performed in order to locate enlarged lymph nodes or organomegalies, and that a blood count and fine-needle aspiration bone marrow biopsy be performed to investigate medullary infiltration. In this case, after these complementary tests, no enlarged lymph nodes, organomegalies or extranodal masses were found, nor was there any involvement of bone marrow or peripheral blood.

CONCLUSION: In summary, PEL is a rare NHL, usually occurring with HIV infection, but our patient was HIV negative, EBV positive. It is most commonly seen as pleural effusion, pericardial effusion or ascites. Generally, it is considered as aggressive NHL and even after chemotherapy prognosis remains poor. Median survival time is 6 to 8 months. A current trial headed by National Cancer Institute is attempting to use combination therapy with antiviral Bortezomib and systemic chemotherapy. Other approaches that have been proposed include targeting latency phase genes such as LANA-1 using small RNA transcripts to silence essential viral genes and augmenting host immunity against HHV-8. It is hoped that this therapy can become the basis for better outcome.

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